REMARKS

Claims 1, 7-9, 11-12, 15, 19-23, 25-36, 38, and 42-44 were pending in the subject application. Claims 12, 15, 23, 31, 32, 34, 38 and 42 are withdrawn from consideration by the Examiner as directed to non-elected species. By this Amendment, Claims 8, 26 and 34 have been canceled without prejudice or disclaimer, and Claims 1, 9, 21, 25, 35, 43 and 44 have been amended. Applicants maintain that the amendments to the claims do not raise an issue of new matter. Support for the claim amendments can be found at least in canceled claim 8 and in the previous version of the claims. Accordingly, entry of the amendments is respectfully requested.

Objections to the Claims

Claims 1 and 35 are objected to because the Examiner indicated that in the phrase "a DNA sequence comprising a smooth muscle specific promoter, smooth muscle alpha actin (SMAA)..., " it is not clear that "smooth muscle alpha actin" necessarily refers to a smooth muscle alpha actin promoter. The claims have been amended to add the word "promoter" after "(SMAA)" as suggested by the Examiner, thereby obviating this objection.

Rejections under 35 U.S.C. §112, First Paragraph

The claims are rejected as not enabled for the full scope of the claims, specifically regarding the type of regulation of smooth muscle tone and the route of administration of the DNA sequence. The claims have herein above been amended to specify that the regulation of smooth muscle tone is enhanced smooth muscle relaxation and that the route of administration of the DNA sequence is direct introduction of the DNA sequence to smooth muscle cells. Accordingly, reconsideration and withdrawal of these rejections are respectfully requested.

Rejections under 35 U.S.C. §112, Second Paragraph

The Examiner indicated that Claims 1 and 35 are indefinite for reciting both a broad recitation "a smooth muscle specific promoter" and "smooth muscle alpha actin" which is a narrower recitation of a smooth muscle specific promoter. The claims have herein above been amended to delete "a smooth muscle specific promoter" and to only recite "a smooth muscle alpha actin (SMAA) promoter..."

The Examiner indicated that Claim 21 is indefinite for reciting "wherein the DNA sequence is introduced using an EYFP vector." The claim has been amended to recite "wherein the DNA sequence is present in an EYFP vector" as suggested by the Examiner.

Accordingly, reconsideration and withdrawal of these rejections are respectfully requested.

Rejections under 35 U.S.C. §102

Claims 1, 7-9, 11, 19-20, 22, 25-30, and 35-36 are rejected under 35 U.S.C. §102(b) as anticipated by Geliebter et al. (U.S. Patent No. 6,150,338) and under 35 U.S.C. §102(e) as anticipated by Geliebter et al. (U.S. Patent No. 7,030,096).

These rejections are respectfully traversed. Neither reference teaches the use of a DNA sequence comprising a smooth muscle alpha actin (SMAA) promoter operably linked to a sequence encoding a potassium channel protein for enhancing penile or urinary bladder smooth muscle relaxation or for treating erectile dysfunction, as required by the amended claims.

Reconsideration and withdrawal of these rejections are respectfully requested.

Rejections under 35 U.S.C. §103(a)

Claims 1, 35, 43 and 44 are rejected as being unpatentable over Geliebter et al. (U.S. Patent No. 6,150,338) in view of Leiden et al. (U.S. Patent No. 6,436,907).

Claims 1 and 21 are rejected as being unpatentable over Geliebter et al. (U.S. Patent No. 6,150,338) in view of pEYFP Vector Information from Clontech.

These rejections are respectfully traversed.

The claimed invention requires the use of a DNA sequence comprising a smooth muscle alpha actin (SMAA) promoter operably linked to a sequence encoding a potassium channel protein for enhancing penile or urinary bladder smooth muscle relaxation or for treating erectile dysfunction. Geliebter et al. do not teach the use of a SMAA promoter. Leiden et al. teach adenovirus-mediated gene transfer to cardiac and vascular smooth muscle and that a SMAA promoter is a preferred vascular smooth muscle promoter. In contrast, Leiden et al. prefer a different promoter for cardiac muscle (col. 3, lines 16-23). Leiden et al. do not teach methods to treat penile or bladder smooth muscle.

Applicants would like to direct the Examiner's attention to two references by the inventors and their colleagues, which were submitted with the Information Disclosure Statement dated April 21, 2010. The paper by Melman et al. (2008) compares the effectiveness of two vectors (pVAX-*hSlo* and pSMAA-*hSlo*) in restoring erectile function in a rat model of erectile dysfunction (Melman A, et al., Gene transfer with a vector expressing Maxi-K from a smooth muscle-specific promoter restores erectile function in the aging rat, Gene Ther. 15(5):364-70, 2008; Epub 2008 Jan 17). The *hSlo* gene encodes maxi-K. In the case of pVAX-hSlo expression, the *hSlo* gene is driven by the cytomegalovirus (CMV) promoter (page 368, bottom of left column). As discussed in the right column on page 367, approximately twice as much gene is expressed from the SMAA promoter compared with the CMV promoter, as was demonstrated using corporal smooth muscle cells *in vitro* (Table 1, on page 365). Consistent with the *in vitro* data, the ability

of pSMAA-*hSlo* transfection to restore erectile function in the aging rat model of erectile dysfunction *in vivo* was similar to or statistically better than pVAX-*hSlo* (Figures 2-5, Table 2). For example, at the lowest level of electrical stimulation of the cavernous nerve (0.5 mA), which innervates erectile tissues of the penis, pSMAA-*hSlo* treated animals showed a statistically significant increase in the ratio of intracavernous pressure (ICP) to blood pressure (BP) when compared to pVAX-*hSlo* treated animals (page 365, last paragraph; Figure 5). More specifically, the ICP/BP ratio exceeded 0.6 at low levels of nerve stimulation for pSMAA-*hSlo* treated animals but not for pVAX-*hSlo* treated animals (Figure 5, Table 2). In addition, the ICP/BP ratio tended to be higher for pSMAA-*hSlo* treated animals than for pVAX-*hSlo* treated animals at all levels of cavernous nerve stimulation (Figure 5, Table 2). As indicated on page 367, right column, the probability of visualizing an erection during cavernous nerve stimulation increases dramatically as the ICP/BP ratio becomes 0.6 or more; thus, these differences are physiologically relevant.

The paper by Christ et al. (2008) demonstrates dramatic improvements in erectile function and sexual behavior following treatment with pSMAA-*hSlo* in cynomologus monkeys with erectile dysfunction secondary to diet-induced atherosclerosis (Christ GJ, et al. Smooth-Muscle-Specific Gene Transfer with the Human Maxi-K Channel Improves Erectile Function and Enhances Sexual Behavior in Atherosclerotic Cynomolgus Monkeys, Eur Urol. Dec 25, 2008 Epub ahead of print). Moreover, an increased responsiveness to intracavernous papaverine injection was observed, and this finding is also consistent with an important role for the smooth muscle cell in the primary mode of action of maxi-K gene transfer. Taken together, these results indicate that increased end organ (i.e., erectile function) *per se*, via smooth muscle-specific gene transfer of the maxi-K channel, may lead to increased sexual function.

The advantageous effects of pSMAA-*hSlo* treatment compared to treatment using a viral vector were not predictable prior to the present invention. For example, as discussed

on page 367, left column, of Melman et al. (2008), it was not clear if lower levels of the gene encoding the potassium channel protein would be expressed using SMAA than with a viral promoter. However, as discussed above, approximately twice as much gene is expressed from the SMAA promoter compared to the CMV promoter. In addition, as further discussed on page 367, it might have been the case that gene expression in multiple cell types contributes to efficacy of treatment. In this scenario, smooth muscle restricted expression using SMAA may not have improved erectile function as effectively as with a non-specific viral promoter, which results in gene expression in multiple cell types. Again, as discussed above, this possibility turned out not to be the case and pSMAA-*hSlo* proved to have advantageous treatment effects compared to pVAX-*hSlo*. Use of the SMAA promoter ensures cell type specific expression of the potassium channel protein, thereby avoiding expression except in the target cell types (smooth muscle cells). Since it has been demonstrated that gene expression in multiple cell types is not required for highly effective treatment, the claimed invention also provides a product with an improved safety profile. These promoter-specific characteristics may have potentially important implications for the efficacy in patients of gene transfer of DNA encoding the potassium channel proteins as set forth in the claims.

Accordingly, the claimed invention provides superior, non-obvious advantages over the teachings of the prior art. Accordingly, reconsideration and withdrawal of these rejections are respectfully requested.

Obviousness-type Double Patenting Rejections

Claims 1, 7-9, 11, 19-20, 22, 25-30, 33 and 35-36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of parent U.S. Patent No. 7,030,096 and over claims 1-9 of U.S. Patent No. 6,150,338.

Claims 43-44 are rejected under the judicially created doctrine of obviousness-type

double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,150,338 in view of Leiden et al. (U.S. Patent No. 6,436,907).

Reconsideration and withdrawal of these rejections are respectfully requested in view of the remarks made herein above regarding the rejections under 35 U.S.C. §§102/103.

Supplemental Information Disclosure Statement

This Supplemental Information Disclosure Statement is being filed to supplement the Information Disclosure Statements filed on May 18, 2006, August 30, 2007 and April 21, 2010 in connection with the subject application. In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the references that are listed on the attached form PTO/SB/08B and attached hereto. These references were cited in an Office Action issued in counterpart Japanese Patent Application No. 2004-316799.

CONCLUSIONS

In view of the amendments and remarks made hereinabove, reconsideration and withdrawal of the objections and rejections in the May 19, 2010 Office Action and passage of the pending claims to allowance are respectfully requested. If there is any minor matter preventing the allowance of the subject application, the Examiner is requested to telephone the undersigned attorney.

A check for $180.00 is enclosed for the fee for submitting an Information Disclosure Statement. No other fee is deemed necessary in connection with the filing of this Amendment and Information Disclosure Statement. However, if any other fee is required to preserve the pendency of the subject application, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 01-1785. Overpayments may also be credited to Deposit Account No. 01-1785.

Respectfully submitted,

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By _____
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